

Amendments to the Claims

1. (Currently amended) An antibody-based fusion protein comprising an N-terminal immunoglobulin (Ig) chain linked to a C-terminal non-Ig protein, the C-terminal non-Ig protein comprising an amino acid substitution introducing alteration to a hydrophobic or non-polar amino acid within 10 amino acids of the N-terminus of the C-terminal non-Ig protein, wherein said antibody-based fusion protein has a longer circulating half-life *in vivo* than a corresponding antibody-based fusion protein without said amino acid alteration substitution.
2. (Currently amended) The antibody-based fusion protein of claim 1, [[48,]] 49, or 51, wherein said amino acid substitution alteration increases the hydrophobicity of said antibody-based fusion protein.
3. (Canceled)
4. (Currently amended) The antibody-based fusion protein of claim [[48,]] 49 or 51, wherein said substitution alteration changes the C-terminal amino acid of the Ig chain.
5. (Previously presented) The antibody-based fusion protein of claim 1, wherein said non-Ig protein is a secreted protein.
6. (Previously presented) The antibody-based fusion protein of claim 5, wherein said non-Ig protein is a mature form of said secreted protein.
7. (Currently amended) The antibody-based fusion protein of claim [[48,]] 49 or 51, wherein the Ig chain comprises part of an Ig heavy chain.
8. (Currently amended) The antibody-based fusion protein of claim [[48,]] 49 or 51, wherein the Ig chain comprises at least the CH2 domain of an IgG2 or an IgG4 constant region.
9. (Canceled)
10. (Canceled)

11. (Currently amended) The antibody-based fusion protein of claim 7, wherein said portion part of an Ig heavy chain further has binding affinity for an immunoglobulin protection receptor.
12. (Previously presented) The antibody-based fusion protein of claim 7, wherein said Ig chain has substantially reduced binding affinity for a Fc receptor selected from the group consisting of Fc γ RI, Fc γ RII and Fc γ RIII, when compared to the binding affinity of an unaltered IgG1 for said Fc receptor.
13. (Previously presented) The antibody-based fusion protein of claim 1, wherein said non-Ig protein is selected from the group consisting of a cytokine, a ligand-binding protein, and a protein toxin.
14. (Original) The antibody-based fusion protein of claim 13, wherein said cytokine is selected from the group consisting of a tumor necrosis factor, an interleukin, and a lymphokine.
15. (Original) The antibody-based fusion protein of claim 14, wherein said tumor necrosis factor is tumor necrosis factor alpha.
16. (Original) The antibody-based fusion protein of claim 14, wherein said interleukin is interleukin-2.
17. (Original) The antibody-based fusion protein of claim 14, wherein said lymphokine is a lymphotoxin or a colony stimulating factor.
18. (Previously presented) The antibody-based fusion protein of claim 17, wherein said colony stimulating factor is a granulocyte-macrophage colony stimulating factor.
19. (Original) The antibody-based fusion protein of claim 13, wherein said ligand-binding protein is selected from the group consisting of CD4, CTLA-4, TNF receptor, and an interleukin receptor.
- 20-23. (Canceled)

24. (Currently amended) The fusion protein of claim 1, [[48,]] 49 or 51, further comprising a linker between said Ig chain and said non-Ig protein.

25-28. (Canceled)

29. (Currently amended) The fusion protein of claim 1 further comprising an amino acid substitution introducing alteration to a hydrophobic or non-polar amino acid within the Ig chain, wherein said antibody-based fusion protein has a longer circulating half-life *in vivo* than a corresponding antibody-based fusion protein without the amino acid substitutions.

30-35. (Canceled)

36. (Currently amended) The fusion protein of claim 4 wherein the C-terminal amino acid of said N-terminal Ig chain is substituted altered to be an amino acid with a non-ionizable side chain.

37-45. (Canceled)

46. (Currently amended) The fusion protein of claim 1, [[48,]] 49, or 51, or 57, wherein said hydrophobic or non-polar amino acid is selected from the group consisting of Leu, Trp, Ala, and Gly.

47. (Previously presented) The fusion protein of claim 1, wherein said hydrophobic or non-polar amino acid is Ala.

48. (Canceled)

49. (Currently amended) An antibody-based fusion protein comprising an N-terminal immunoglobulin (Ig) chain linked to a C-terminal non-Ig protein, the Ig chain comprising an IgG1, IgG2, IgG3, IgG4, IgA, IgM, IgD, or IgE constant domain and an amino acid substitution introducing alteration to a hydrophobic or non-polar amino acid within 10 amino acids from the C-terminus of the Ig chain, wherein said antibody-based fusion protein has a longer circulating

half-life *in vivo* than a corresponding antibody-based fusion protein without said amino acid alteration substitution.

50. (Currently amended) The antibody-based fusion protein of claim 49 wherein the constant domain comprises at least one or more of a CH1, CH2, or CH3 domain.

51. (Currently amended) An antibody-based fusion protein comprising an N-terminal immunoglobulin (Ig) chain linked to a C-terminal non-Ig protein, the Ig chain comprising:

at least one of a CH2 and CH3 domain; and

an amino acid sequence that is non-natural within 10 amino acids from its C-terminus, the non-natural amino acid sequence comprising an amino acid substitution introducing alteration to a hydrophobic or non-polar amino acid, wherein the antibody-based fusion protein has a longer circulating half-life *in vivo* than a corresponding antibody-based fusion protein without said amino acid substitution alteration.

52. (Previously presented) The antibody-based fusion protein of claim 51 wherein the Ig chain is an IgG1, IgG2, IgG3, IgG4, IgA, IgM, IgD, or IgE chain.

53. (Currently amended) The antibody-based fusion protein of claim 4 wherein the Ig chain comprises the CH2 domain of the IgG2 constant region and the a C-terminal amino acid is a lysine is substituted with a nonpolar or hydrophobic amino acid.

54. (Currently amended) The antibody-based fusion protein of claim 53, wherein the C-terminal amino acid lysine is altered to an alanine.

55. (Previously presented) The antibody-based fusion protein of claim 53, wherein the non-Ig protein is a cytokine.

56. (New) An antibody-based fusion protein comprising an N-terminal immunoglobulin (Ig) chain linked to a C-terminal non-Ig protein, the Ig chain comprising at least one of a CH2 and a CH3 domain, and the C-terminal non-Ig protein comprising an amino acid alteration within 10 amino acids of the N-terminus of the C-terminal non-Ig protein, the alteration introducing an

amino acid selected from the group consisting of Leu and Trp, wherein said antibody-based fusion protein has a longer circulating half-life *in vivo* than a corresponding antibody-based fusion protein without said amino acid alteration.

57. (New) An antibody-based fusion protein comprising an N-terminal immunoglobulin (Ig) chain linked to a C-terminal non-Ig protein, the Ig chain comprising an amino acid substitution within 10 amino acids from the C-terminus, the substitution replacing a charged amino acid with a hydrophobic or non-polar amino acid, wherein the antibody-based fusion protein has a longer circulating half-life *in vivo* than a corresponding antibody-based fusion protein without said amino acid substitution.

58. (New) An antibody-based fusion protein comprising an N-terminal immunoglobulin (Ig) chain linked to a C-terminal non-Ig protein, the N-terminal Ig chain comprising an amino acid substitution within 10 amino acids from the C-terminus of the Ig chain, the substitution introducing a hydrophobic or non-polar amino acid selected from the group consisting of Ala, Gly and Trp, wherein the antibody-based fusion protein has a longer circulating half-life *in vivo* than a corresponding antibody-based fusion protein without said amino acid substitution.

59. (New) An antibody-based fusion protein comprising an N-terminal immunoglobulin (Ig) chain linked to a C-terminal non-Ig protein, the N-terminal Ig protein comprising a CH3 domain, wherein the CH3 domain comprises a deletion of a charged amino acid within 10 amino acids of the C-terminus of the CH3 domain, wherein said antibody-based fusion protein has a longer circulating half-life *in vivo* than a corresponding antibody-based fusion protein without said deletion.